Published in final edited form as:
Qual Life Res. 2014 February ; 23(1): 75–88. doi:10.1007/s11136-013-0436-3.

Impact of diagnosis of diabetes on health-related quality of life among high risk individuals: the Diabetes Prevention Program outcomes study

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Abstract

Purpose—The purpose of this study is to assess if diagnosis of type 2 diabetes affected health-related quality of life (HRQoL) among participants in the Diabetes Prevention Program/Diabetes Prevention Program Outcome Study and changes with treatment or diabetes duration.

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Clinical trials Registry DPPOS: NCT00038727 and DPP: NCT00004992.

A complete list of the DPPOS Research Group investigators is shown in the Appendix 2.

Methods—3,210 participants with pre-diabetes were randomized to metformin (MET), intensive lifestyle intervention (ILS), or placebo (PLB). HRQoL was assessed using the SF-36 including: (1) 8 SF-36 subscales; (2) the physical component (PCS) and mental component summary (MCS) scores; and (3) the SF-6D. The sample was categorized by diabetes free versus diagnosed. For diagnosed subgroup, mean scores in the diabetes-free period, at 6 months, 2, 4 and 6 years post-diagnosis, were compared.

Results—PCS and SF-6D scores declined in all participants in all treatment arms (P <.001). MCS scores did not change significantly in any treatment arm regardless of diagnosis. ILS participants reported a greater decrease in PCS scores at 6 months post-diagnosis (P <.001) and a more rapid decline immediately post-diagnosis in SF-6D scores (P = .003) than the MET or PLB arms. ILS participants reported a significant decrease in the social functioning subscale at 6 months (P <.001) and two years (P <.001) post-diagnosis.

Conclusions—Participants reported a decline in measures of overall health state (SF-6D) and overall physical HRQoL, whether or not they were diagnosed with diabetes during the study. There was no change in overall mental HRQoL. Participants in the ILS arm with diabetes reported a more significant decline in some HRQoL measures than those in the MET and PLB arms that developed diabetes.

Keywords

Diagnosis of diabetes; Health-related quality of life; Pre-diabetes; Type 2 diabetes mellitus; Prevention

Introduction

Quality of life is a health outcome measured as a combination of physical and social functioning, and perceived physical and mental well-being [1, 2]. Having a serious chronic disease such as diabetes can exert a negative impact on health-related quality of life (HRQoL) [3–9]. Few studies, however, have investigated the impact of the diagnosis of type 2 diabetes on HRQoL. Earlier research reported minimal negative impact following a diagnosis, with these effects diminishing within a year [6, 10–12]. These minimal effects may be the result of not understanding the seriousness of the disease, the fact that negative impact diminishes as the individual adapts to living with the condition, and the limited impact of early type 2 diabetes on physical well-being [13–15].

Less is known about how HRQoL changes over time following diagnosis, especially as diabetes duration increases, but before the onset of complications. Moreover, no study to date has reported the effect on HRQoL of type 2 diabetes diagnosis in persons who are made *aware* of both their personal risk for developing the disease and how serious diabetes is. The impact of diagnosis on HRQoL in persons who are actively seeking to reduce their personal risk is unknown.

Participants in the Diabetes Prevention Program Outcome Study (DPPOS) are an ideal group to study these issues [16]. To participate, they had to have impaired glucose tolerance (IGT), elevating their risk of developing diabetes, and were made aware of their diabetes risk. Regular glucose testing allowed relatively precise determination of diabetes onset, and participants were followed for several years after being informed they had developed diabetes. The DPPOS cohort is large, varied in age, and race/ethnicity. It also randomized subjects to one of three study conditions: an intensive lifestyle intervention, use of a medication, or a placebo control. This study design enables exploration of the effect of diabetes prevention interventions on HRQoL following diabetes diagnosis.

This is a unique and heretofore never studied population with regards to how diagnosis of type 2 diabetes may impact QOL. Previous studies have not been able to accurately ascertain when the disease actually occurred. In this study, we could do so within six months. Based on previous research which has investigated how diagnosis impacts QOL ratings over time, we hypothesize that that our sample would report initially having a negative impact on QOL to the diagnosis of diabetes followed by a return to values near baseline within the first year. [6, 10–12] In addition, since our sample is older (mean age at baseline of 50 at baseline) and was followed for multiple years, and there is a literature documenting that QOL declines with advancing age, we also hypothesized that decreases in QOL would be faster following diagnosis than compared to similar aged subjects who remained diabetes free. Finally, we hypothesized that participation in the different study interventions would influence perceptions of QOL following diagnosis. Specifically, we hypothesized that subjects in the intensive lifestyle arm would react more negatively due to the degree of behavior change required of them in this condition to reduce their risk as compared to subjects in either the medication or placebo arms.

Design and methods

The DPP enrolled individuals at high risk for type 2 diabetes at 27 clinic centers. DPP methods and results are described in detail elsewhere [16–18]. The protocol is available at http://www.bsc.gwu.edu/dpp. At each DPP center, an institutional review board approved the protocol and all participants gave written informed consent.

The DPP randomized 3,234 participants. Participants ≥25 years of age had a BMI of ≥24 kg/m^2 (≥22 kg/m^2 in Asian Americans), and a plasma glucose concentration of 95–125 mg/dl (5.3–6.9 mmol/l) in the fasting state (≤125 mg/dl in American Indian centers) and 140–199 mg/dl (7.8–11.0 mmol/l) 2 h after a 75-g oral glucose load. Exclusion criteria included medication that might contribute to weight loss, conditions that could reduce ability to participate in the DPP, or inability to complete the 3-week run-in period during which participants took placebo medicines and recorded their usual eating and physical activity patterns.

Of this sample, 3,210 had SF-36 forms collected at baseline and are included in this analysis. This included 1,070 in intensive lifestyle (ILS); 1,066 in metformin (MET); and 1,074 assigned to Placebo (PLB) [19]. The subjects were followed for a median of 8.97 years.

Interventions

Participants were randomized to one of three interventions: metformin (MET arm), a placebo pill (PLB arm), or an intensive lifestyle modification program (ILS arm). Goals for ILS participants were to achieve and maintain a reduction of ≥7 % of initial body weight through a calorie-controlled, low-fat diet and to engage in physical activity of moderate intensity, for ≥150 min per week [20].

Measures

SF-36—The short-form health-related quality of life (SF-36) survey was administered as a measure of overall HRQoL at enrollment in the DPP and annually thereafter. The SF-36 enables measurement of generic health-related quality of life at three levels: 8 subscales that represent distinct domains of health; component scores for physical and mental health; and a single utility measure that is frequently used in cost-effectiveness analyses. The 8 domains of health are as follows: physical functioning (ability to engage in physical activities), role-physical (impact of physical health on role-based activities), bodily pain (severity and

impact), general health (global assessment of health), vitality (energy, fatigue), social functioning (physical or emotional health impact on social activities), role-emotional (impact of emotional health on role performance), and mental health (depression, anxiety). Higher scores on all SF-36 scales indicate more favorable levels of functioning. A change of 2 points in these subscales is also considered a clinically significant change [21, 22].

The eight subscales were used to generate two composite scores: the Physical Component Summary (PCS; physical functioning, role-physical, body pain, and general health) and the Mental Component Summary (MCS; vitality, social functioning, role-emotional, and mental health subscales). Both subscale and composite scores were norm-based with a mean of 50 and a standard deviation of 10 in the normative population. The PCS and MCS sub-scales range from 0 to 100, with higher scores indicating better quality of life relevant to either mental or physical components. A two-point change in either the MCS or PCS score is considered clinically significant [21].

The eight domains of the SF-36 can also be converted into a six-dimensional health state classification called the SF-6D [22] to derive a single summary preference or utility-based HRQoL measure. The six dimensions are physical functioning, role limitations, social functioning, pain, mental health, and vitality. The SF-6D has a range of score from 0.29 to 1.00 with 1.00 indicating “full health.” A difference of 0.04 in SF-6D scores is considered clinically significant [23].

Diabetes was diagnosed using the 1997 American Diabetes Association criteria [24] based on an annual oral glucose tolerance test (fasting level ≥7.0 mmol/l and/or a plasma glucose level ≥11.1 mmol/l) or a semiannual fasting plasma glucose test (level ≥ 7.0 mmol/l). Diagnosis required a confirmation test within 6 weeks [16]. After a confirmed diagnosis of diabetes, participants were informed and advised to see their usual health care provider for additional treatment considerations. All participants who developed diabetes remained in the DPP trial to track long-term secondary outcomes and continued to complete annual questionnaires following their diagnosis.

Demographic and clinical characteristics of the study participants, which might affect the HRQoL, were also collected in the study [25–27]. This includes measures of obesity (BMI, weight, and waist-to-hip ratio), comorbid conditions, blood pressure, albumin-to-creatinine ratios, microalbuminuria, lipids (non-HDL cholesterol) physical activity (average physical activity hours per week, MAQ Leisure Activity, and LoPar Leisure Activity) [27], medications that could affect quality of life, and demographic factors (age, sex, race/ethnicity, marital status, economic status, and smoking history).

Statistical methods

We studied changes in SF-36 PCS and MCS scores, SF-36 sub-scale scores, and SF-6D scores. HRQoL changes among those who developed diabetes were compared with changes among those who had not developed diabetes by data closure and the diabetes-free period of those who later developed diabetes.

Two time axes were employed in this study. At the time of enrollment of DPP (as discussed above), all participants were diabetes free and their randomization time was used as time zero for the diabetes-free period. For those who developed diabetes, we employed a second time axis where the onset of diabetes was set as time zero. Then, for models using the second time axis, all diabetes-free person-times was used as the reference set. This diabetes-free person-time included the complete follow-up of participants who had not developed diabetes by data closure and the prior-diabetes time interval of people who developed diabetes during the follow-up. It is important to note that the occurrence of diabetes happens

at different time points in follow-up. Therefore, a participant would be in the diabetes-free group first and then enters the diagnosed group after he/she was diagnosed with diabetes. A plot explaining the two time axes is provided in the section “Appendix 1”.

Short-term (<6 months) and long-term (up to 6 years) changes in HRQoL were estimated separately within each treatment arm. Repeated HRQoL measurements were collected over DPP and DPPOS follow-up. Such longitudinal data provide opportunity to study the trend of HRQoL over time within persons as well as differences between persons, which are usually modeled by growth curve models [28]. Specifically, we employed linear mixed regressions because the HRQoL measures are continuous and approximately normal. Besides, correlations induced by repeated measures from the same participant were modeled by a compound symmetry correlation structure [29], which assumes a constant positive correlation coefficient between measurements from the same participant and independence between measurements from different participants. Four different time intervals post-diagnosis (<6, 6 months–2, 2–4, 4–6 years post-diagnosis) were used as categories of different durations of diabetes in the analysis to assess differences in the impact of diagnosis over time. Covariates for adjustment included demographic factors (age, race, sex), baseline socioeconomic status (marriage, employment, and income), baseline health conditions (HRQoL, Beck Depression Index score, Beck Anxiety Index score, smoking status, BMI, fasting plasma glucose level, and 2-hour plasma glucose level) and years since randomization in diabetes-free participants. All test results are presented without adjustment for multiplicity. Except the HRQoL values for the diabetes-free group (Fig. 1, left panel), which are raw average values, all HRQoL measurements post-diabetes occurrences are predicted from the linear mixed models assuming all covariates taking the average values in the DPP cohorts.

The sample sizes within all three treatment groups decreased as DPPOS follow-up got longer due to enrollment of participants over time. Besides, the sample sizes within all treatments also decreased as the diabetes duration got longer (see Table 1), and there are fewer diabetic participants in ILS group than the other groups. We assume the HRQoL patterns among participants who developed diabetes later in the study will not be systematically different from those who developed diabetes earlier, after adjusting for the baseline characteristics in the linear mixed model, that is, missing at random.

Results

At baseline, there were no significant differences among treatment arms on any level of HRQoL or covariate (Table 1). SF36 component and utility scores by diabetes status and treatment arm

Figure 1a–c shows SF-6D, MCS, and PCS scores for participants who remained diabetes free (left) and participants diagnosed with diabetes (right). Notice that the plots on the left use the DPP follow-up time scale, that is, number of years since DPP randomization on the x-axis. The HRQoL measures on the right are plotted over number of years since diabetes diagnosis. All values on the left panel are observed average values within each treatment group, and all values on the right panel are predicted from the linear mixed models discussed in the Statistical methods section.

The graph for the SF-6D scores (Fig. 1a) shows that when diabetes-free participants showed little decline in scores for approximately three years of participation in the study and that participants in the ILS treatment actually reported a slight increase in scores from baseline to one year. Beginning at year three, however, participants in all the treatment groups that remained diabetes free show a progressive decline in SF-6D scores. This is in contrast to

participants who were diagnosed with diabetes during the study shown on the graph on the right. The scores post-diabetes diagnoses show a more rapid decline when compared to the diabetes-free participants. In addition, participants in the lifestyle group who were diagnosed reported a more severe reduction in the period immediately following diagnosis ($P = .003$) compared to the other groups. The difference between the intervention groups, however, was not statistically different, possibly due to the decreasing sample sizes as the diabetes duration increased.

Table 2 shows the average decrease in SF-6D scores over the entire follow-up period was approximately 0.01 per year ($P < .001$) among both diabetes-free participants and those who developed diabetes. The decline in SF-6D scores did not reach clinical significance in any treatment arm for participants who developed diabetes or for those who did not. These data indicate that our sample did not experience a rapid decline that returned to baseline values as it was hypothesized. Rather, they show a negative decline that continued over the course of the study period.

MCS scores (Fig. 1b) among DM-free participants did not change significantly in any treatment arm. In addition, MCS scores did not change significantly over the entire follow-up period in those diagnosed with diabetes, with no significant difference among groups, though scores in the ILS arm declined immediately following diagnosis, before returning to levels close to those for the other two treatment arms.

Figure 1c shows PCS scores for participants when they were diabetes free (left panel) and those who developed diabetes during the trial. During the DM-free period, participants in the ILS group showed a marked increase ($P < .001$) in scores from baseline to one year, then a gradual decline from year one to six. Participants in the MET and PLB groups remained stable over the course of the study until year five when MET participants reported a decrease followed by a sharp increase in year six. The fluctuation could result from the small sample sizes with six years follow-up. PCS scores showed a progressive decline following diabetes diagnosis among participants in all treatment arms, with no significant differences among treatment groups in PCS score change over time. Among the DM-free participants, the slopes (−0.26) are not statistically different between treatments and much smaller than the slopes post-diabetes ($P < .001$). In those diagnosed, the slope in ILS is faster (−0.46) than the other two groups (−0.40 and −0.39). However, a test for the interaction between slope and treatment in the diagnosed participants does not reach statistical significance ($P = .639$). Figure 1 provided evidence for our second hypothesis that decreases in QOL would be faster following diagnosis than compared to similar aged subjects who remained diabetes free in the PCS measures, but not in the MCS measures.

Finally, we speculated that the finding that ILS participants reported more negative scores post-diabetes than those in the other groups might be due to their greater age (because ILS delayed the onset of diabetes). We tested for age at diagnosis in each group and saw no significant difference between the ages at DM onset across the three treatments. Average age of diabetes onset was 57.53 years in the ILS, 57.37 in the MET, and 56.34 in the PLB groups.

SF-36 subscale scores by diagnosis status and treatment arm

Research has suggested that relying solely on the MCS–PCS summary scores may be misleading in understanding how they reflect HRQoL [30, 31]. Thus, to characterize changes in HRQoL at the level that is closest to participant experience, we analyzed each of the SF-36 subscale scores. All analyses shown were adjusted for covariates. We report here only the subscales that showed significant differences between the three treatments for diagnosed participants.

Physical Component Subscales Among diagnosed participants, analyses of the four subscales that comprise the PCS (physical functioning, role-physical, general health, and bodily pain), showed that the role-physical scores decline progressively over time in all three groups (Fig. 2a). These declines from diagnosis to the period 2–4 year post-diagnosis are of clinical significance with all changes ≥2 points (P = .007, .008, .081 in the ILS, MET, and PLA groups, respectively). Lifestyle participants also showed a greater decline in Role-Physical scores in the first six months following diagnosis compared to the other two groups (P = .026), with further declines after 2 years with diabetes (P = .068). The data for the other three subscales did not show significant differences.

Mental Component Subscales Analyses of the four subscales that comprise the MCS (i.e., Vitality, Role-Emotional, Mental Health, and Social Functioning) showed that participants in the MET and PLB groups showed little change post-diagnosis, whereas participants in the ILS intervention reported greater and clinically significant declines in Social Functioning at 6 months (P = .001) and 24 months (P = .001) post-diagnosis (Fig. 2b). The scores from the ILS participants did rise at 2–4 years and were similar to those of participants in the other groups, but fell at the 4–6 year time period. A decline in Role-Emotional scores was also significantly greater in the ILS group at all time points post-diagnosis; however, these differences did not reach clinical significance until the period 0.5–2 years (P = .190) and again at 4–6 years (P = .063).

There were no significant differences between ILS participants and participants in the other two treatment groups in vitality and mental health score changes. The Role-Emotional score in the ILS group is approximately one unit lower than the others over time post-diabetes, but this difference does not reach statistical significance. Collectively, the data regarding treatment effects support our hypothesis that subjects in the intensive lifestyle arm would react more negatively than subjects in the other two treatment arms, but in somewhat selective ways. In particular, subjects in the lifestyle arm did report a more negative effect initially following diagnosis on quality of life for the PCS scales and some of the mental component subscales.

Discussion

This is the first study able to determine with relative accuracy when diabetes actually developed. This allows us to control for exposure effects that result from previous studies that cannot determine how long persons actually had diabetes before they had HRQoL assessed. In addition, unlike previous research, which has largely been cross-sectional, this is the first study that followed a cohort for several years following the diagnosis.

There are several findings of note. We found a statistically significant, persistent, and progressive negative decline in measures of overall health state (SF-6D scores) and overall physical HRQoL (PCS scores) in all treatment arms following diabetes diagnosis, with no change in measures of overall mental HRQoL (MCS scores). These data were not supportive of the hypothesis that HRQoL would return to near baseline levels after initial diagnosis, which is what has been shown in previous research. They suggest that other factors play a significant role in how persons with prediabetes who participate in a prevention intervention react to the revelation that they have in fact developed type 2 diabetes.

The pattern of change on all measures of HRQoL following diabetes diagnosis (i.e., a decline in PCS and SF-6D scores, with no change in MCS scores) mirrored the pattern of change for the same measures among diabetes-free DPP participants. This suggests that other factors beyond diabetes diagnosis (e.g., study burden) may have influenced HRQoL over time. DPP treatment burden was substantial. Participants had to provide many

biological samples and fill out numerous questionnaires every 6 months for several years. Aging could also have negatively affected HRQoL. The average age at entry into the trial was 51; thus, many of the participants may have begun to experience decrements in their physical capacity that is associated with increasing age. It is known that PCS scores decline with age and are negatively affected by the onset of complications other than those of diabetes such as arthritis, heart disease, and emphysema. In this context, the declines observed here are similar to those in other studies, albeit which did not focus on diabetes [32, 33]. In this context, the data partially support the study hypothesis that declines would result from aging, but failed to support that this resulted from the discovery of diabetes per se.

At baseline, participants reported PCS and MCS scores of 50 and 54, respectively. These are higher than mean scores for general US population [32]. This may reflect the eligibility criteria for inclusion in the study. Participants were initially screened to reduce the influence of such factors as comorbid conditions that would negatively impact HRQoL such as clinical depression. It is possible that over time participants tended to "regress to the mean" in their assessments of HRQoL.

We also observed significant changes among those diagnosed with diabetes in the ILS group at the level of the PCS component score and Role-Physical subscale compared to the MET or PLB groups. These finding may reflect the ways in which the diagnosis of diabetes (and the consequent changes in medical and behavioral management required) affects participants' perceived ability to physically perform (e.g., have you had any of the following problems with your work or other regular daily activities *as a result of your physical health*?).

We found no negative impact of diabetes diagnosis at the level of component scores for mental HRQoL (MCS scores), but examination of the individual SF-36 subscales that combine to form this component revealed significant differences in the ILS arm for the Social Functioning and Role-Emotional subscales following diagnosis. Both of these subscales ask respondents to report the extent to which physical or mental health status interferes with their ability to engage in social tasks or perform these tasks at expected levels (e.g., Did not do work or other activities as carefully as usual?). Consistent with previous studies [31, 32], this finding suggests that the MCS component scores were not as sensitive in capturing meaningful changes in mental health HRQoL as the individual subscale scores. Previous studies have reported a negative mental health impact on HRQoL following diagnosis, but most studies report this resolving as the patient gains more experience with treating the disease, usually within one year [6, 10, 11]. We saw, however, a decrease in HRQoL that persisted for multiple years and in fact continued to decrease. The change observed is consistent with other measures of the patient experience of diabetes (e.g., diabetes distress, hassles), that is, diabetes represents a psychological burden that has the capacity to adversely affect individuals emotionally and socially over the long-term.

The finding that the greatest declines in HRQoL were observed in the PCS rather than the MCS scores is not surprising. While it is logical to assume that the impact of a diagnosis of diabetes would be most strongly expressed through measures of mental and social status, there is increasing evidence that PCS scores decline as people age [32, 33]. This finding may also reflect a study effect; in that, all participants received extensive social support from DPP/DPPOS staff and were provided extensive exposure to counseling and education services. This may have acted to minimize the negative emotional impact of the diagnosis.

The study did support the hypothesis that participating in the ILS arm of the trial would result in a more negative impact on HRQoL. Participants in the ILS arm who were

diagnosed with diabetes reported a greater decline on the SF-6D than participants in other two treatment groups, particularly in the immediate period (i.e., 0–6 months from diagnosis) following diagnosis. In addition, diabetes-free ILS participants reported an increase on the PCS scale in the period closest to their most active participation in the lifestyle intervention. This may reflect the significant improvements in the level of physical activity and weight loss resulting from their efforts at lifestyle modification.

The general finding that participants in the ILS group showed a more pronounced decline in HRQoL scores is of note. Participants in lifestyle were asked to adopt new behaviors that included significant changes in their diet and patterns of physical activity. Thus, they were adopting new lifestyle behaviors that in almost all cases represented significant departures from their baseline status. In contrast, participants in both the metformin and placebo control groups were not asked to adopt new behaviors except taking medication, a behavior that is both simpler to adopt and probably more familiar to the average participant. Participants in ILS group may have experienced more intense disappointment when, in spite of actually losing weight, they still developed diabetes. One way in which their disappointment may have magnified is from the reactions of others to their “discovery” of diabetes. Significant others may have expressed a reaction to the diagnosis in terms of the effort expended by the lifestyle participant: “e.g., too bad, you worked so hard… you lost so much weight.” This may have acted to intensify the perception of failure and loss in spite of the effort expended to prevent the disease. It may also have resulted in some degree of experiencing stigma associated with being labeled as diabetic and being perceived as a failure. This interpretation is supported in part by the greater changes in the social function scores in the lifestyle group. As seen in Fig. 2, their initial reaction is quite pronounced but approaches the levels of other participants after sometime to habituate to the diagnosis that has occurred.

These data suggest that the HRQoL associated with the diagnosis of diabetes and participation in an intensive lifestyle intervention is a complex phenomenon. This is the first study to investigate the impact on HRQoL in a population with known risk who were actively trying to prevent developing the disease. These data are different from the previous studies that suggest that a diagnosis of diabetes has a minimal impact on HRQoL and tended to resolve within a year [6, 10, 11]. Prior research, however, has not focused on populations who were particularly aware of their risk status and exercising considerable efforts to reduce their risk. In addition, previous studies also assessed HRQoL well after the diagnosis of diabetes was made.

Study strengths and limitations warrant consideration. Strengths include the large, racially and ethnically diverse population; the definitive assessment of glucose tolerance and diabetes; and that data were collected about health-related quality of life repeatedly from baseline over several years. In addition, the timing of diagnosis of diabetes could be pinpointed to a 6 month period, which is a considerable advance over studies that assess perceived impact of diagnosis retroactively and rely on medical records that may not accurately capture the time of diagnosis or when diabetes was actually present. It is also the first study to investigate the impact of diagnosis on a population actively trying to reduce their risk of developing the disease. Most important, we were able to compare changes in HRQoL between diabetes-free participants and those who developed diabetes.

Limitations include reliance on generic measures of HRQoL to define the impact of diagnosis. These measures may not specifically address dimensions of HRQoL that are linked to the diagnosis of diabetes. Also, the sample was deliberately chosen to be relatively free of mental health issues, notably depression and anxiety disorders, which are known to be more prevalent in the general population and particularly in a population of persons with diabetes. Thus, it is unknown how a sample with a more widely distributed occurrence of

mental health issues would respond. Extrapolation of these results to other populations that are not participating in a major clinical trail warrants some caution. Future studies should examine the perception of expectations for prevention associated with different treatment modalities. Such studies are feasible with large populations (e.g., HMOs). This study is the first to quantify how a person's HRQoL may change as he or she moves from prediabetes to diabetes. Such information is critical to build a model for diabetes progression that can be used for evaluating the cost-effectiveness of interventions for preventing diabetes, as well as to understand how the time horizon for observing changes in quality of life might impact the findings of these analyses. The negative impact of diabetes diagnosis on HRQoL also supports the need to develop strategies to help newly diagnosed patients to cope with diabetes immediately after diagnosis and also emphasize the importance of secondary prevention to reduce diabetes burden as they age.

Acknowledgments

The Research Group gratefully acknowledges the commitment and dedication of the participants of the DPP and DPPOS. During the DPPOS, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health provided funding to the clinical centers and the Coordinating Center for the design and conduct of the study, and collection, management, analysis, and interpretation of the data (U01 DK048489). The Southwestern American Indian Centers were supported directly by the NIDDK, including its Intramural Research Program, and the Indian Health Service. The General Clinical Research Center Program, National Center for Research Resources, and the Department of Veterans Affairs supported data collection at many of the clinical centers. Funding was also provided by the National Institute of Child Health and Human Development, the National Institute on Aging, the National Eye Institute, the National Heart Lung and Blood Institute, the Office of Research on Women's Health, the National Center for Minority Health and Human Disease, the Centers for Disease Control and Prevention, and the American Diabetes Association. Bristol-Myers Squibb and Parke-Davis provided additional funding and material support during the DPP, Lipha (Merck-Sante) provided medication, and LifeScan Inc. donated materials during the DPP and DPPOS. We thank the thousands of volunteers in this program for their devotion to the goal of diabetes prevention. LifeScan Inc., Health O Meter, Hoechst Marion Roussel, Inc., Merck-Medco Managed Care, Inc., Merck and Co., Nike Sports Marketing, Slim Fast Foods Co., and Quaker Oats Co. donated materials, equipment, or medicines for concomitant conditions. McKesson BioServices Corp., Matthews Media Group, Inc., and the Henry M. Jackson Foundation provided support services under subcontract with the Coordinating Center. The opinions expressed are those of the investigators and do not necessarily reflect the views of the funding agencies.

Appendix 1

See Fig. 3.

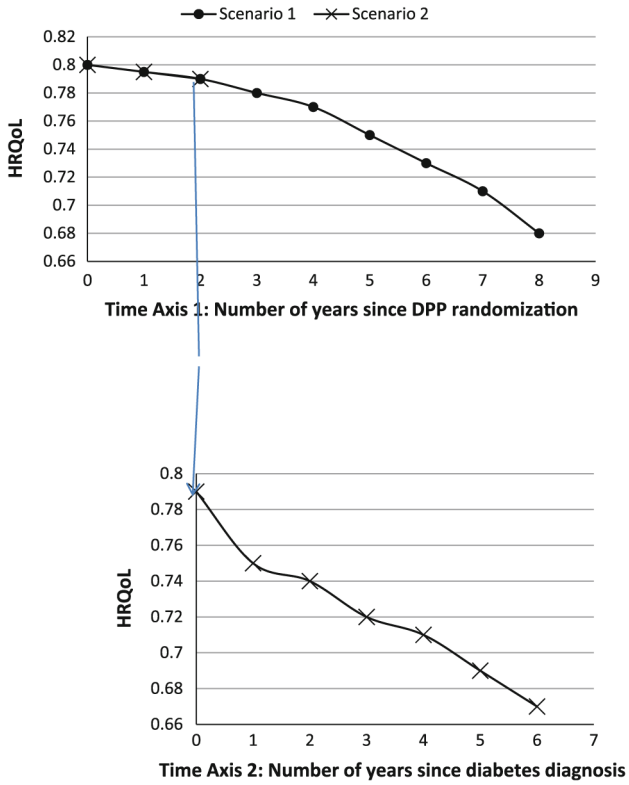

Fig. 3.
Two hypothetical scenarios a DPP participant could experience and the corresponding time axis for each scenario. First scenario: the participant remained diabetes-free throughout the follow-up and stayed on the time since DPP randomization axis. Second scenario: the participant was diagnosed of diabetes two years after DPP randomization and jumped to the second time axis of time since diabetes diagnosis

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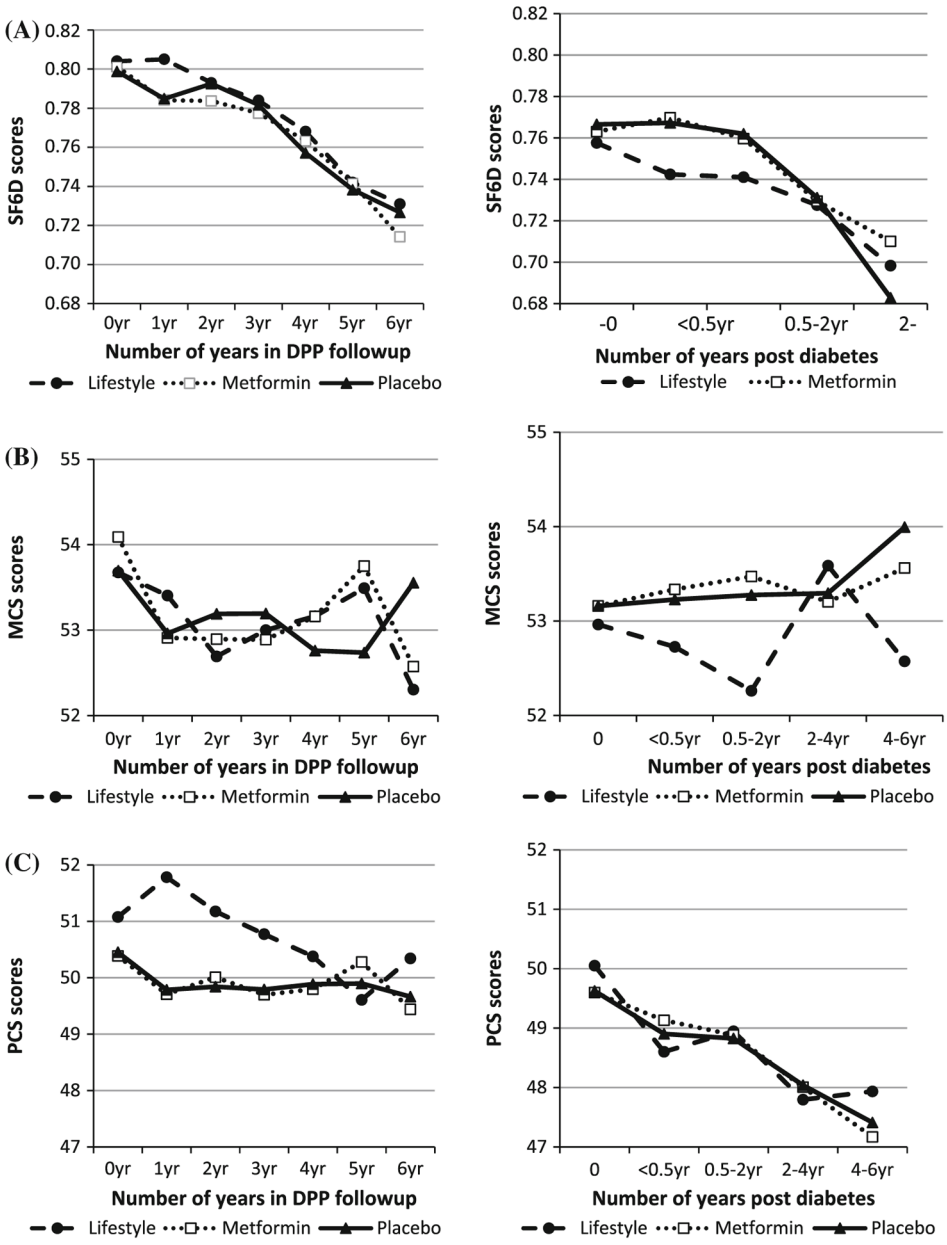

Fig. 1.

Average treatment-specific HRQoL scores over DPP follow-up among diabetes-free participants * time (*left*); Predicted average treatment-specific HRQoL scores post-diabetes (*right*)

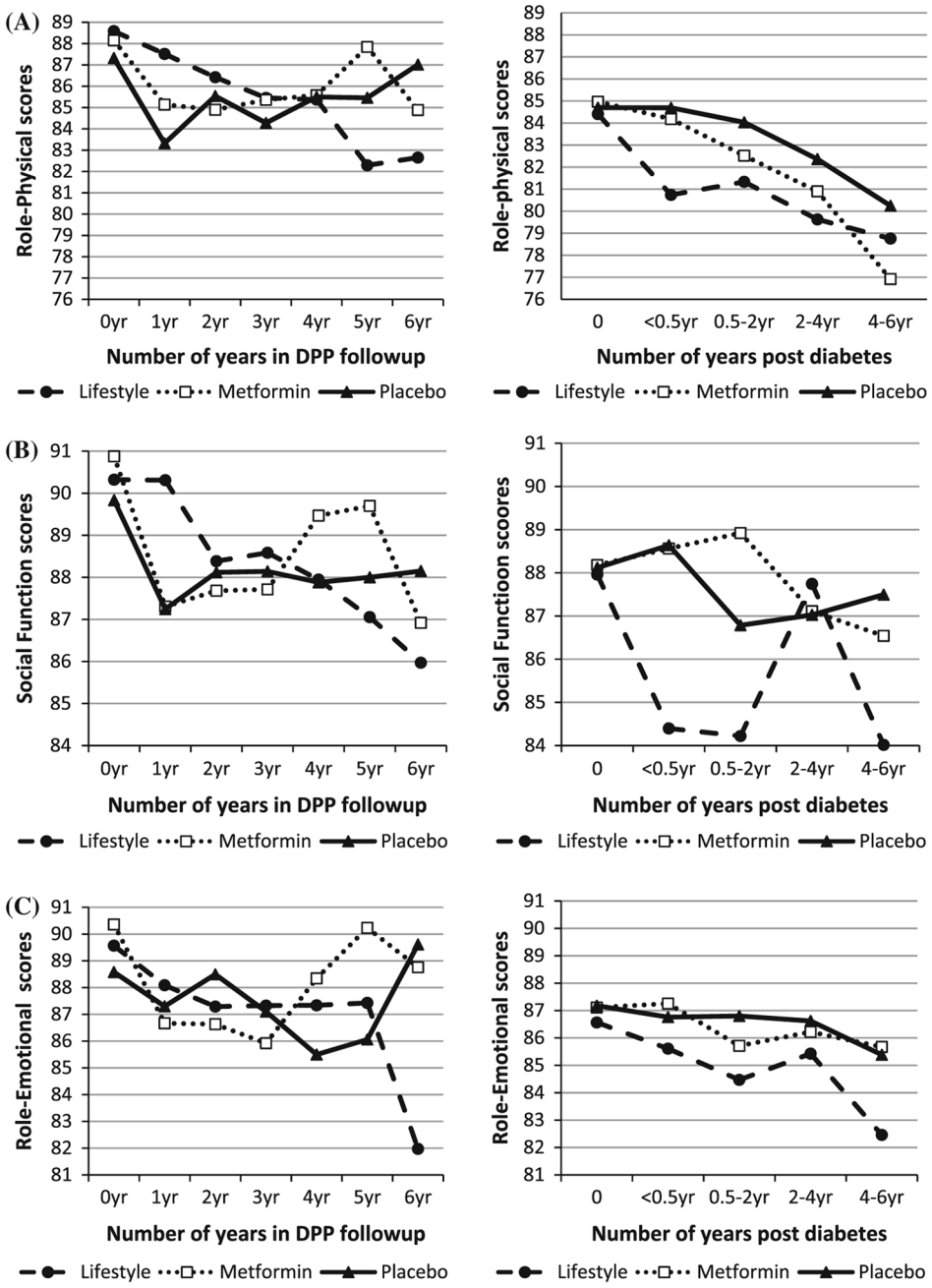

Fig. 2.

Average treatment-specific HRQoL subscale scores over DPP follow-up among diabetes-free participants * time (*left*); Predicted average treatment-specific HRQoL subscale scores post-diabetes (*right*)

Table 1

Sample characteristics at baseline (no significant differences between groups) and sample sizes with different diabetes durations

Variable	Lifestyle	Metformin	Placebo	Total/Avg
Sample size				
Baseline	1,070	1,066	1,074	3,210
0–0.5 year post-DM	262	327	389	978
0.5–2 year post-DM	223	318	379	920
2–4 year post-DM	182	231	302	715
4–6 year post-DM	116	141	157	414
Demographic characteristics				
Age	50.6 (11.3)	50.9 (10.3)	50.3 (10.4)	50.6 (10.7)
Female	729 (68 %)	705 (66 %)	742 (69 %)	2,176 (68 %)
White	576 (54 %)	599 (56 %)	579 (54 %)	1,754 (55 %)
African-American	203 (19 %)	218 (20 %)	220 (20 %)	641 (20 %)
Hispanic	178 (17 %)	161 (15 %)	168 (16 %)	507 (16 %)
American Indian	58 (5 %)	52 (5 %)	59 (5 %)	169 (5 %)
Asian	55 (5 %)	36 (3 %)	48 (4 %)	139 (4 %)
Married	654 (61 %)	658 (62 %)	671 (62 %)	1,983 (62 %)
Employed	779 (73 %)	821 (77 %)	785 (73 %)	2,385 (74 %)
Annual household income ($10 K)	5.3 (1.7)	5.4 (1.7)	5.3 (1.8)	5.30 (1.7)
Clinical characteristics				
Smoke	70 (7 %)	71 (7 %)	84 (8 %)	225 (7 %)
Body mass index (kg/m^2)	33.9 (6.8)	33.9 (6.6)	34.1 (6.7)	34.0 (6.7)
Beck depression score	4. 6 (4.5)	4.5 (4.4)	4.6 (4.7)	4.6 (4.6)
Beck anxiety inventory score	4.1 (5.1)	3.9 (4.9)	4.0 (5.0)	4.0 (5.0)
Fasting glucose (mg/dL)	106.3 (8.1)	106.5 (8.5)	106.8 (8.4)	106.5 (8.3)
2-hour glucose (mg/dL)	164.4 (16.9)	165.2 (17.2)	164.5 (17.1)	164.7 (17.1)
Outcome variables				
Physical functioning	85.8 (16.6)	84.7 (17.5)	85.6 (17.0)	85.4 (17.0)
Role-physical	88.5 (25.4)	87.7 (26.1)	87.9 (26.5)	88.0 (26.0)
Body pain	78.7 (20.1)	78.2 (19.4)	77.6 (19.8)	78.2 (19.8)
General health	76.1 (16.3)	75.2 (16.5)	76.2 (16.7)	75.8 (16.5)
Vitality	65.0 (18.8)	65.2 (18.2)	65.5 (18.8)	65.2 (18.6)
Social functioning	90.5 (17.1)	90.6 (17.1)	90.7 (16.4)	90.6 (16.9)
Role-emotional	89.9 (24.5)	89.7 (25.0)	89.5 (24.8)	89.7 (24.8)
Mental health	81.9 (13.8)	82.3 (13.5)	82.4 (13.7)	82.2 (13.7)
Physical component score (PCS)	50.6 (6.9)	50.1 (7.3)	50.3 (7.2)	50.3 (7.1)
Mental component score (MCS)	53.8 (7.6)	54.1 (7.7)	54.0 (7.4)	54.0 (7.5)
SF-6D utility score	0.80 (0.10)	0.80 (0.10)	0.80 (0.10)	0.80 (0.10)

* Categorical characteristics are described as number (%); continuous characteristics are expressed as mean (standard deviation)

Table 2

Linear trend of HRQoL over time before and after diabetes diagnosis

	DM-free		Post-DM					
	Change rate	*P* value	Lifestyle		Metformin		Placebo	
			Change rate	*P* value	Change rate	*P* value	Change rate	*P* value
SF6D	−0.0107	<.001	−0.0097	<.001	−0.0108	<.001	−0.0104	<.001
MCS	−0.05	.007	0.13	.063	0.08	0.162	0.04	.415
PCS	−0.26	<.001	−0.46	<.001	−0.39	<.001	−0.40	<.001

The *P* values are for the hypothesis that the corresponding slope equals to 0. The interaction between treatment and the slope over time post-DM is not significantly different from zero (*P* value = .608, .639, and .584 for SF6D, PCS, and MCS, respectively). However, the difference between the slopes before and after diabetes diagnosis (DM-free vs. post-DM) is significantly different from zero in PCS and MCS (*P* value = .577, <.001 and .002 for SF6D, PCS, and MCS, respectively)

* All change rates are in the unit of points per year